REMARKS

With the entry of this Amendment, claims 23-28 and 31-50 are now pending in the application.

I. Definiteness Rejection

The Examiner has rejected claims 27 and 32 under 35 U.S.C. § 112, second paragraph, as indefinite for allegedly failing to include essential method steps. For example, in the claimed immunoassay, the Examiner believes that it is essential to provide assay steps and the requisite reagents necessary to perform the steps. The Examiner suggests amending the claims to recite the attachment of a suitable antigen on a microtiter plate, the addition of a biological sample from an HIV-1-infected patient, an incubation period, a rinsing step to remove unbound immunoglobulin, addition of labeled anti-Ig antibody to detect the immune complex, a rinsing step to remove non-specific label, and a detection step employing enzymatic reagents.

The Examiner has also rejected claims 28 and 33 as indefinite for similarly failing to set forth allegedly essential method steps for methods of eliciting neutralizing antibodies. The Examiner believes that simply introducing the antibodies into the mammal is insufficient. The Examiner suggests amending the claims to recite preparation of the immunogen in a suitable form, inclusion of an adjuvant, an immunization regimen, and removal of samples from the mammal to assay the affinity and activity of the antibodies.

In response to both of these rejections, Applicants have amended claims 27, 28, 32, and 33 to recite method steps. Support for the amendments to claims 27 and 32 can be found on pages 32-33 of the specification. Support for the amendments to claims 28 and 33 can be found on pages 16-17 of the specification. Applicants therefore request that the Examiner withdraw this rejection.

II. Written Description Rejection

The Examiner has rejected claims 23-28 and 31-39 under 35 U.S.C. § 112, first paragraph as allegedly lacking written description. The Examiner argues that the original application does not provide adequate support for the broadly claimed genus of immunogenic polypeptide fragments comprising HIV-1_{MAL} epitopes of 5-150 amino acid residues wherein at least one amino acid residue is substituted at one of the specific positions.

The Examiner provides three reasons for his conclusion. First, he argues that the disclosure fails to identify any specific HIV-1_{MAL} immunogenic fragments of the claimed lengths and substitutions. Second, the Examiner argues that the disclosure fails to perform any type of comparison wherein specific immunogenic fragments from isolate MAL are identified and acceptable amino acid substitutions are performed. Third, the Examiner alleges that the disclosure fails to provide adequate support for MAL-specific polypeptides of the recited lengths. The Examiner disagrees with Applicants' argument that figures 3E-F provide support for the claimed invention.

Previously Presented Claims

Applicants had amended the claims in the last response because the Examiner was concerned about whether the claims provided information on which amino acids were mutated and what peptide lengths were supported in the application. With respect to the peptide length, Applicants point to the statement in the specification that peptides comprising or **consisting of** the conserved regions (which have the lengths of 21, 43, 79, 94, and 131, respectively) are included in the invention. See page 23. This very specific disclosure provides support for peptides having the claimed lengths. Applicants maintain that it is not necessary to recite the length (for example 21 amino acids) when a peptide with that length is disclosed in the specification (for example 680-700). The same concept is conveyed, irrespective of how it is described.

With respect to the location of the mutations, Applicants maintain their positions that the identity of the mutations encompassed by the invention could be ascertained by considering Figure 3. Applicants believe that comparison of the various Env sequences in Figure 3 highlights positions where an amino acid is substituted in all of the sequences designated LAV_{BRU}, ARV2, and LAV_{ELI} when compared to LAV_{MAL}. This shows that this particular amino acid is not required for immunogenicity. This information assists one in understanding which Env sequences were not required for immunogenicity and shows that this was understood by the inventors at the earliest filing date, as mentioned in the specification on page 16, line 30 through page 17, line 14. The claims include a listing of these nonconserved amino acids, which are targets for mutation. The specification states on page 23 that "[p]roteins containing or

consisting of the 'well conserved stretches' are of particular interest." This statement implies that nonconserved amino acids, such as those provided in claim 23 as derived from Figure 3, are not essential for function of the peptides and may be mutated.

New Claim 40

Applicants added new claim 40 to recite that the peptides comprise certain conserved sequences. The conserved sequences are recited on page 23, and the text following the sequences recites that "[p]roteins containing or consisting of the 'well conserved stretches' are of particular interest." Therefore, Applicants believe peptides comprising these conserved regions are adequately supported in the specification.

Furthermore, reference to the conserved sequences, such as those recited on page 23 of the specification, provides a substantial link between the structure of the claimed peptide and its recited function as conserved sequences are well recognized for maintaining a protein's function. *See* specification page 12, lines 11 to 14, stating that the inventors already knew that well-conserved stretches are "associated with important biological function." Additionally, *see* specification page 16, lines 8 to 16, stating that the inventors had already identified the immunogenic capacity of the peptides consisting of or comprising the well conserved stretches of the Env protein of HIV-1.

Comparison to *Enzo Biochem*

It is useful to compare the present application to a fairly recent Federal Circuit decision, *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956 (Fed. Cir. 2002). While the written description issue in that case was not decided, but was instead remanded to

the district court for further consideration, the Federal Circuit elaborates on what types of situations might provide written description support for biotechnology inventions.

In that case, the claims were directed to nucleic acid probes that selectively hybridize to the DNA of *Neisseria gonorrhoeae*, when compared to a similar bacteria *Neisseria meningitides*. The patentee, Enzo, had identified three nucleic acid probes meeting the claim limitations and had deposited those probes. Enzo argued that the claims were supported by the written description because of the disclosed correlation of the function of hybridization with the bacterial DNA. *Id.* at 967. As strains of the two bacteria were publicly available and could be used to identify which probes would meet the limitations of the claims, the Federal Circuit stated that whether the claims were supported by the written description was a factual one and could not be decided against the patentee in summary judgment. In doing so, the Federal Circuit relied on the Written Description Guidelines issued by the U.S.P.T.O. The Guidelines state that written description can be met by

> Show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

Id. at 964 (quoting Guidelines, 66 Fed. Reg. at 1106).

The Federal Circuit continued by describing an example provided in the guidelines of claims to an isolated antibody to a known antigen, given the well defined structural properties of antibodies, the functional characteristics of antibody-antigen binding, and the high level of scientific understanding in that particular field. *Id.* It

concluded, before remanding the case, that the written description requirement would be met for all of the patent claims "if the functional characteristic of preferential binding to *N. gonorrhoeae* over *N. meningitidis* were coupled with a disclosed correlation between that function and a structure that is sufficiently known or disclosed." *Id.* The Federal Circuit continued by stating "[b]ecause the claimed nucleotide sequences preferentially bind to the genomic DNA of the deposited strains of *N. gonorrhoeae* and have a complementary structural relationship with that DNA, those sequences, under the PTO Guidelines, may also be adequately described." *Id.* at 968.

Thus, the court remanded the case to determine "whether a reasonable fact-finder could conclude that the claimed sequences are described by their ability to hybridize to structures that, while not explicitly sequenced, are accessible to the public. Such hybridization to disclosed organisms may meet the PTO's Guidelines stating that functional claiming is permissible when the claimed material hybridizes to a disclosed substrate." *Id.*

Like *Enzo*, the present invention is defined by an established structural-functional relationship. The specification clearly recites a correlation between the conserved sequences and the function of the claimed peptides. It states that the peptides containing the well conserved regions are of "particular interest for the production of immunogenic compositions and (preferably in relation to the stretches of the <u>env</u> protein) of vaccine compositions against the LAV-1 viruses." *See* specification, pages 12 and 23. As *Enzo* states, the question is whether a person of skill in the art would consider the subject matter of the claimed invention clearly described. As conserved

regions of proteins have been well recognized as contributing to the function of those proteins, Applicants believe that a skilled artisan would have envisioned the class of peptides in claim 40 comprising those conserved regions. Applicants believe that a skilled artisan would also have envisioned the class of peptides in the previously presented claims having mutations in nonconserved amino acids. Applicants assert that this combination of structural and functional features having a disclosed correlation between that function and a sufficiently described structure is sufficient to provide written description support for this invention.

Therefore, Applicants request that the Examiner withdraw this rejection.

III. Additional Claims

Applicants have added new claims 41-49 to encompass methods of using the peptides recited in U.S. Patent No. 6,426,073. Corresponding method claims were canceled from that application during prosecution and were not able to be rejoined before issuance.

IV. Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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Dated: December 9, 2004

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